## **LISTING OF CLAIMS**

This listing of claims will replace all prior versions, and listings, of the claims in the application.

- (Currently Amended) An artificial low-density lipoprotein (LDL) particle comprising an
  outer phospholipid monolayer and a solid lipid core, wherein the outer phospholipid
  monolayer comprises at least one recombinant-apolipoprotein and the solid lipid core
  contains at least one therapeutic agent linked to cholesterol by an ester bond.
- 2. (Currently Amended) The artificial LDL particle of claim 1, wherein the at least one apolipoprotein is ApoE.
- 3. (Currently Amended) The artificial LDL particle of claim 1, wherein the at least one apolipoprotein is ApoE3.
- 4. (Original) The artificial LDL particle of claim 1, wherein the at least one therapeutic agent is selected from the group consisting of: amino acids, peptides, proteins, carbohydrates and lipids.
- 5. (Cancelled)
- 6. (Original) The artificial LDL particle of claim 1, wherein the outer phospholipid monolayer comprises phosphatidylcholine and at least one apolipoprotein.
- 7. (Original) The artificial LDL particle of claim 6, wherein the at least one apolipoprotein is ApoE.
- 8. (Original) The artificial LDL particle of claim 1, wherein the particle has a diameter between about 15 and 50 nm.
- 9. (Original) The artificial LDL particle of claim 1, wherein the particle has a diameter between about 20 and 30 nm.
- 10. (Original) The artificial LDL particle of claim 1, wherein the particle has a density between about 1.00 and 1.07 g/ml.

- 11. (Original) The artificial LDL particle of claim 1, wherein the particle has a density between about 1.02 and 1.06 g/ml.
- 12. (Original) The artificial LDL particle of claim 1, wherein the particle has a serum stability of at least two hours.
- 13. (Original) The artificial LDL particle of claim 1, wherein the particle is transported across the blood-brain barrier (BBB) by transcytosis.
- 14. (Original) The artificial LDL particle of claim 1, wherein the particle has at least a 3-fold greater uptake specificity for brain compared to liver.
- 15. (Currently Amended) The artificial LDL particle of claim 1, wherein the at least one therapeutic agent is a conjugate formed between cholesterol and adriamycin linked to cholesterol by an ester bond.
- 16. (Currently Amended) The artificial LDL particle of claim 1, wherein the at least one therapeutic agent is a conjugate formed between cholesterol and tetracycline linked to cholesterol by an ester bond.
- 17. (Cancelled)
- 18. (Cancelled)
- 19. (Previously Presented) An artificial low-density lipoprotein (LDL) particle for delivery of an agent across the blood-brain barrier comprising an outer phosphatidylcholine monolayer, a solid lipid core comprising fatty acyl-cholesterol esters, and ApoE in the outer monolayer.
- 20. (Original) The artificial LDL particle of claim 19, wherein the solid lipid core further comprises cholesterol.
- 21. (Original) The artificial LDL particle of claim 19, wherein the ApoE in the outer monolayer is ApoE3.

- 22. (Original) A composition for delivery of an agent across the blood-brain barrier comprising the artificial LDL particle of claim 1 and a pharmaceutically acceptable carrier.
- 23. (Original) A composition for delivery of an agent across the blood-brain barrier comprising the artificial LDL particle of claim 4 and a pharmaceutically acceptable carrier.
- 24. (Original) A composition for delivery of an agent across the blood-brain barrier comprising the artificial LDL particle of claim 5 and a pharmaceutically acceptable carrier.
- 25. (Currently Amended) A conjugate comprising cholesterol linked <u>by an ester bond</u> to adriamycin or tetracycline.
- 26. (Cancelled)
- 27. (Currently Amended) The conjugate of claim 25 26, wherein the cholesterol is linked to adriamycin through an ester linkage.
- 28. (Previously Presented) The conjugate of claim 27, wherein the conjugate has the structure in Figure 5.
- 29. (Currently Amended) The conjugate of claim <u>25</u>, <del>26</del>, wherein the cholesterol is linked to tetracycline through an ester linkage.
- 30. (Previously Presented) The conjugate of claim 29, wherein the conjugate has the structure in Figure 6.
- 31. (Original) The artificial LDL particle of claim 4, wherein the therapeutic agent is selected from the group consisting of: neurotrophic factors, growth factors, enzymes, neurotransmitters, neuromodulators, antibiotics, antiviral agents, antifungal agents and chemotherapeutic agents.
- 32. (Cancelled)

- 33. (Original) The artificial LDL particle of claim 1, wherein the outer phospholipid monolayer further comprises one or more oxysterols and/or an additional apolipoprotein selected from the group consisting of ApoB and ApoE4.
- 34. (Previously Presented) A method of producing an artificial low-density lipoprotein (LDL) particle of claim 1 comprising the steps of: 1) suspending phospholipids containing conjugated or unconjugated therapeutic agent in a buffer solution; 2) sonicating the solution to form the outer phospholipid monolayer and solid lipid core; and 3) adding a solution comprising at least one apolipoprotein, wherein the at least one apolipoprotein is ApoE and is incorporated into the outer phospholipid monolayer.
- 35. (Original) The method of claim 34, wherein the artificial LDL particles produced have a diameter between 10 and 50 nm.
- 36. (Original) A method for delivery a substance across the blood-brain barrier, said method comprising administering an effective amount of the composition of claim 22 to a mammal in need thereof.
- 37. (Original) A method for delivery a substance across the blood-brain barrier, said method comprising administering an effective amount of the composition of claim 23 to a mammal in need thereof.
- 38. (Original) A method for delivery a substance across the blood-brain barrier, said method comprising administering an effective amount of the composition of claim 24 to a mammal in need thereof.
- 39. (Original) A kit for delivering substances across the blood-brain barrier, said kit comprising a container containing the composition of claim 22 and instructions for use.
- 40. (Original) A kit for delivering substances across the blood-brain barrier, said kit comprising a container containing the composition of claim 23 and instructions for use.
- 41. (Original) A kit for delivering substances across the blood-brain barrier, said kit comprising a container containing the composition of claim 24 and instructions for use.